PIL Title:	Tofacitinib citrate (5 mg)
PIL Date:	10 January 2018
Country:	Malaysia
References:	Malaysia LPD dated 03 January 2017
Reason for Change:	PIL update as per current effective LPD

XELJANZ FILM-COATED TABLETS

Tofacitinib citrate (5 mg)

What is in this leaflet

What XELJANZ is used for

XELJANZ is used for the treatment of adult patients with moderately to severely active rheumatoid arthritis in whom methotrexate did not work well or have had difficulty handling methotrexate due to its side effects. It may be used as single agent or in combination with methotrexate or other nonbiologic disease-modifying antirheumatic drugs (DMARDs).

- It is not known if XELJANZ is safe and effective in people with Hepatitis B or C.
- XELJANZ is not for people with severe liver problems.
- It is not known if XELJANZ is safe and effective in children

How XELJANZ works

XELJANZ contains the active substance tofacitinib which block proteins called JAK. It preferentially inhibits JAK1 & JAK3 which prevents the activation and reduce the activity of several inflammatory signals called cytokines, including IL-2, -4, -6, -7, -9, -15, -21 and type-1 interferons. These inflammatory signals are important in the activation, function and multiplication of our body's white blood cells. Hence, blocking these signals will help to control our body's immune responses involved in rheumatoid arthritis.

By blocking excess inflammation, XELJANZ helps to reduce symptoms such as pain and swelling in your joints and can improve your performance of daily tasks.

Before you use XELJANZ

- *When you must not use it*

Do not take XELJANZ if:

- You are allergic to tofacitinib citrate or any of the other ingredients of this medicine
- You have an active severe infection such as tuberculosis or pneumonia
- You have severe liver problems

- *Before you start to use it*

Talk to your doctor or pharmacist regarding these before taking XELJANZ

- If you think you have an infection or have symptoms of an infection such as fever, sweating, chills, muscle aches, cough, shortness of breath, new phlegm or change in phlegm, weight loss, warm, red or painful skin or sores on your body, difficulty or pain when swallowing, diarrhea or stomach pain, burning when you urinate or urinating more often than normal, feeling very tired
- If you are being treated for an infection
- If you get a lot of infections or have infections that keep coming back
- If you have tuberculosis or have been in close contact with someone with tuberculosis. Your doctor will test you for tuberculosis before starting XELJANZ
- If you have any condition that increases your chance of infection (e.g. diabetes, HIV/AIDS, or a weak immune system)
- If you have or have had hepatitis B or hepatitis C (viruses that affect the liver). The virus may become active while you are taking XELJANZ. Your doctor may do blood tests for hepatitis before you start treatment with XELJANZ and while you are taking XELJANZ
- If you ever had any type of cancer previously. XELJANZ can affect the immune system and may increase your risk of certain cancers. Lymphoma and other cancers have been reported in patients treated with XELJANZ
- If you have raised blood pressure, raised cholesterol levels, diabetes; these factors need to be monitored while receiving XELJANZ
- If you have had an inflammation of the large intestine (diverticulitis) or ulcers in your stomach or intestines
- If you have had severe narrowing of the stomach or intestines
- If you have lung problems
- If you have severe kidney problems
- If you have liver problems
- If you are planning to get vaccinated, tell your doctor. Live vaccines should not be given when taking XELJANZ. Vaccination should occur 4 weeks before starting XELJANZ.
- If you are pregnant, think you may be pregnant or are planning to become pregnant, ask your doctor for advice before taking this medicine. It is not known if XELJANZ will harm an unborn baby. XELJANZ should not be

used during pregnancy unless clearly necessary. Tell your doctor right away if you become pregnant while taking XELJANZ.
- It is not known if XELJANZ is found in breast milk. If you are breastfeeding, you and your doctor should discuss to decide if you will take XELJANZ or breastfeed. You should not do both.

Monitoring tests performed before and during treatment with XELJANZ: Your doctor should perform a blood test before you start taking XELJANZ to determine your white blood cell (neutrophil or lymphocyte) count, red blood cell count (hemoglobin) and lipid (cholesterol) levels. This blood test should be repeated after 4 to 8 weeks of taking XELJANZ (for neutrophils, hemoglobin and lipids) and then repeated every 3 months thereafter (for lymphocytes, neutrophils and hemoglobin).

If your white blood cell (neutrophil or lymphocyte) count or red blood cell count is too low, or if your liver test results are too high, your doctor might stop or change your dose of XELJANZ and/or other treatments for a period of time until they normalize. If your lipid (cholesterol) levels increase, your doctor will need to treat your cholesterol levels separately to ensure it is well controlled.

- *Taking other medicines*
  Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. Some medicines should not be taken with XELJANZ. If taken with XELJANZ, they could cause an inappropriate level of XELJANZ in your body, and the dose of XELJANZ may require adjustment. You should tell your doctor if you are using medicines (taken by mouth) that contain any of the following active substances:
  - antibiotics such as clarithromycin and rifampin, used to treat bacterial infections
  - fluconazole and ketoconazole used to treat fungal infections

  XELJANZ is not recommended for use with biologic treatments for RA or with medicines that depress your immune system (i.e. azathioprine, tacrolimus or cyclosporine). Taking XELJANZ with these medicines may increase your risk of infection.

How to use XELJANZ
- *How much to use*
  Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure. The recommended dose is 5 mg twice a day. Your doctor may reduce the dose if you have liver or kidney problems. You should not increase or decrease the dose on your own.

- *When to use it*
  XELJANZ is taken by mouth. Take your medication at the same time every day (one tablet in the morning and one tablet in the evening). You can take XELJANZ with or without food.

- *How long to use it*
  Continue taking XELJANZ for as long as your doctor recommends. You should not stop taking XELJANZ without discussing this with your doctor. If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

- *If you forget to use it*
  Consult your doctor or pharmacist on what you should do if you forget to take it. Take the missed dose as soon as you remember. However, if it is almost time for the next dose (within 6 hours), wait until then to take the medicine and skip the missed dose. Do not take 2 tablets to make up for it.

- *If you use too much (overdose)*
  Contact your doctor or pharmacist immediately and go to the Emergency Department of your nearest hospital. You will be monitored for signs and symptoms of adverse reactions.

While you are using XELJANZ
- *Things you must do*

- Take your medicine exactly as your doctor has told you.
- Tell your doctor immediately if you become pregnant
- Tell your doctor if you wish to breastfeed
- Tell all the doctors and pharmacists treating you that you are taking XELJANZ, or if you will be taking any other medicines
- Take all your blood tests regularly and on time.
- If you experience allergic reactions such as chest tightness, wheezing, severe dizziness or light headedness, swelling of the lips, tongue or throat, itching or skin rash when taking XELJANZ, or soon after taking XELJANZ, tell your doctor immediately
- If you have any kind of infection or if you have any symptoms of an infection (as described above) tell your doctor immediately, especially if you are aged 65 years and above, have diabetes and are taking medicines that can reduce your immunity such as corticosteroids.
- If you experience weakness in your muscles, worsening shortness of breath or develop yellow skin, nausea or vomiting, tell your doctor immediately.
- If you develop any symptoms of ulcers in your stomach or intestines or symptoms of inflammation of the large intestine (diverticulitis) such as fever, abdominal pain, blood in the stool

and unexplained changes in bowel habits, tell your doctor. It is rare for people taking XELJANZ to get holes in their stomach or intestine, however this happens most often in people who had a history of diverticulitis and also in people who take non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids or methotrexate.

- If you develop any type of cancer, tell your doctor.
  Talk to your doctor if you do not feel better or if you feel worse when taking XELJANZ.
- If new skin lesions appear during or after therapy or if existing lesions change appearance, tell your doctor.
- Keep this leaflet. You may need to read it again. If you have further questions, ask your doctor or pharmacist.

- *Things you must not do*

- Do not stop taking XELJANZ unless advised by your doctor.
- Do not take any new medicines without consulting your doctor.
- This medicine has been prescribed for you only. Do not pass it on to others, even if their signs of illness are the same as yours. It may harm them.

- *Things to be careful of*

Driving and using machines
No formal studies have been carried out to study the effects of XELJANZ on the ability to drive and use machines.

Side Effects
Like all medicines, this medicine can cause side effects, although not everybody gets them.

Possible serious side effects include serious infections (pneumonia, cellulitis, shingles, urinary tract infection) and allergic reactions, that may be life-threatening.

The most common infections are:
- upper respiratory tract infections
- nasopharyngitis
- urinary tract infections

Other side effects which have been observed with XELJANZ are listed below:

Diarrhea, nasopharyngitis, upper respiratory tract infections , headache, high blood pressure (hypertension), low red blood cell count (anemia), inflammation of the large intestine (diverticulitis), dehydration, poor sleep, abnormal sensation of skin (paresthesia), shortness of breath or difficulty breathing, stomach (belly) pain (which may be from inflammation of the stomach lining), vomiting, nausea, indigestion, fat accumulate in liver cells, rash, redness and itching of skin, joint pain, tendon inflammation, joint swelling, pain in the muscles, fever, fatigue (tiredness), swelling of the feet and hands.
Cancer of lungs, breast, gastric, colorectal, renal cell, prostate, lymphatic system, melanocytes (pigment causing cells).
Low white blood cell count , increased liver enzymes, increased cholesterol, increased serum creatinine.

You may report any side effects or adverse drug reactions directly to the National Centre for Adverse Drug Reaction Monitoring by calling Tel: 03-78835550, or visiting the website npra.moh.gov.my (Public → Reporting Medicinal Problems / Side Effects / AEFI / Vaccine Safety).

Storage and Disposal of XELJANZ
- *Storage*

Keep XELJANZ out of the sight and reach of children.

Store XELJANZ below 30°C.

Do not use XELJANZ after the expiry date stated on the carton, bottle, or blister.

Store XELJANZ in its original package in order to protect from moisture. Do not repackage it.

Do not use this medicine if you notice the tablets show visible signs of deterioration (for example, are broken or discoloured).

- *Disposal*

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to dispose medicines you no longer use as any unused product or waste material should be disposed of in accordance with local requirements. These measures will help protect the environment.

Product Description
- *What it looks like*

Film-coated tablets: XELJANZ 5 mg film-coated tablets are white round immediate release film-coated tablet debossed with 'Pfizer' on one side and 'JKI 5' on the other.

Package in foil / foil blister containing 14 or 56 film-coated tablets.
Some product strengths or pack sizes may not be available in your country.

- *Ingredients*
- *Active ingredient*:
Tofacitinib

The tablets for oral administration contain tofacitinib 5 mg dosage strength.

- *Inactive ingredients*:
Tablet Core: Microcrystalline cellulose, lactose monohydrate, croscarmellose sodium, magnesium stearate
Film Coat for 5 mg tablets: Opadry® II White (33G28523) containing hypromellose, titanium dioxide,

lactose monohydrate, macrogol, triacetin

- *MAL Number*
XELJANZ FILM-COATED TABLETS 5 MG - MAL14075067AZ

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